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Highly controlled gene expression using combinations of a tissue-specific promoter, recombinant adenovirus and a tetracycline-regulatable transcription factor.

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Controllable gene expression is a desirable feature both in gene therapy protocols and for the study of gene function in animals and plants. We have exploited the modular character of the tetracycline (tc)-regulatable genetic switch to show that its components can be encoded by any combination of recombinant adenovirus and/or transgenic mice. Transgenic mice were constructed that express the tc-regulatable trans-activator tTA muscle specifically. These were injected with recombinant adenovirus expressing a luciferase reporter controlled by the tTA-regulatable promoter. Virus injected into muscle, but not into a control organ (brain) resulted in luciferase activity. Conversely, injection of tTA producing adenovirus into mice that were transgenic for a trkB/Fc fusion protein gene under tc promoter control resulted in swift expression of serum trkB/Fc receptor-body. Both modes of gene induction were fully inhibited by administration of tc. We demonstrate that a careful choice of these tools allows exquisite in vivo control over transgene expression in a temporal, tc-regulatable, topical and tissue-specific manner.

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